Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 1-2, 8, 10-12 and 42 are pending in the application, with claim 1 being the independent claim. No new matter is added to the present application by the foregoing amendment, which are fully supported in the specification as originally filed, and its entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Objection to the Claims

In the Office Action, at page 2, the Examiner objected to claims 8 and 9 for containing limitations drawn to non-elected groups. By the foregoing amendment, Applicants have cancelled claim 9 and have amended claim 8 to address the Examiner's concern. Therefore, Applicants respectfully request that the objection to the claims be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

In the Office Action, at page 2, the Examiner rejected claims 1, 2 and 8-12 under 35 U.S.C. § 112, first paragraph for allegedly not being enabled for variants or fragments of SEQ ID NO:1. Applicants respectfully traverse this rejection. Solely in an effort to expedite prosecution, and without acquiescing with the propriety of the rejection, however, Applicants have canceled claim 9, thus rendering its rejection moot. Also in the interest of expediting

the allowance of the above-captioned application, Applicants have amended the other rejected claims to make explicit that which was implicit in the claims by adding functional language, *i.e.*, the phrase "biologically active" to describe the claimed peptides. Therefore, Applicants have addressed the Examiner's concern at page 3, first full paragraph regarding "functional language."

In one aspect, the invention claimed in the above-captioned application relates to minimized, biologically active PTH peptides. The Examiner alleges that Applicants only teach the amino acid sequence of SEQ ID NO:1, and that the specification does not provide guidance on use of the variant polypeptides. The Examiner states: "Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible muteins of SEQ ID NO: 1." Office Action at 4. Applicants disagree and respectfully direct the Examiner's attention to, *inter alia*, Example 2, Table 2; Example 6, Table 3; Example 7, Table 4; and Figures 1-7, in which the biological activity of several muteins and fragments of a polypeptide having the sequence of SEQ ID NO:1 is measured in different experimental systems.

Applicants note that they are not required to provide experimental examples of each and every functional derivative that would fall under the scope of the claims. *See, e.g., Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1237, quoting *In re Angstadt,* 537 F.2d 498, 502, 190 U.S.P.Q. (BNA) 214, 218 (CCPA 1976) ("it is not necessary that a patent applicant test all the embodiments of his invention. . . . what is necessary is that he provide a disclosure sufficient to enable one skilled in the art to carry out the invention commensurate with the scope of his claims."). Applicants have discovered, *inter alia*, that PTH and PTHrP peptides can be minimized, while retaining signaling and binding activity, by mutating certain

residues, and they provide ample guidance as to the position and nature of the substitutions that would enable a peptide to maintain biological activity.

Applicants further note that the polypeptides claimed in the above-captioned application are short. Therefore, a polypeptide having a sequence that is at least 90% identical to SEQ ID NO: 1 would have no more than a single amino acid substitution, and thus the pool of the potentially resulting muteins is very limited. Because Applicants provide ample guidance as to which substitutions could be tolerated, and because the number of muteins that are encompassed by the current claims is finite and small, Applicants respectfully assert that, once a person skilled in the art is in possession of Applicants' disclosure, that person will need to do no more than routine experiments to produce compounds encompassed by the scope of the claims.

In view of the foregoing amendments and explanations, Applicants respectfully request that the rejection of claims 1-2, 8 and 10-12 under 35 U.S.C. § 112, first paragraph, be withdrawn.

In the Office Action, at page 5, the Examiner alleged that "the Specification only sets forth that the polypeptide of SEQ ID NO: 1 was active in cells expressing the PTH-2 receptor and in osteoblast cells, however, there is not a correlation between these activities and the treatment of a disease state. . . . it would require one of skill in the art to determine the function of the variant polypeptides, then determine whether this function would correlate to the treatment of a disease state, thus requiring undue experimentation." Office action at 5-6. Applicants disagree.

As described in the "Background of the Invention" section of the Specification, PTH is a major regulator of calcium homeostasis, the disruption of which can produce many clinical disorders such as bone disease, anemia, renal impairment, ulcer, myopathy and

neuropaty. Specification at 1-2. PTH administration has been shown to also promote bone formation, and PTH derivatives are considered to be prime candidates for new and effective therapies for osteoporosis. Specification at 6. As discussed in the Specification, it is also known that PTH exerts its influence on calcium homeostasis through binding and initiating signaling through the PTH cell-surface receptors. Specification at 4-5. Thus, the specification provides specific disease states to be treated by the peptides of the present invention (e,g., conditions resulting from calcium imbalance, osteoporosis, etc.); a mechanism to test the efficacy of these peptides; and a description of how and in what amounts these peptides should be administered to a patient in need thereof. Applicants respectfully assert that they are not required to provide examples of actual patients successfully treated by the pharmaceutical composition of claim 12 and that they have provided examples that show PTH biological activity in peptides of SEQ ID NO:1 in cell systems that are model systems for treating calcium imbalance conditions.

"When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application. . . . " *In re Wright*, 999 F.2d 1557, 1561-2 (Fed. Cir. 1993). Applicants respectfully assert that, in view of the detailed teachings of the specification discussed above, the Examiner has not met his burden of setting out a prima facie case for the lack of enablement of claim 12. Therefore, Applicants respectfully request that the rejection of claim 12 under 35 U.S.C. § 112 be withdrawn.

In the Office Action on page 6, the Examiner rejected claims 2 and 8-12 under 35 U.S.C. § 112, first paragraph for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art

that the inventors had possession of the claimed invention at the time that the application was filed. Applicants respectfully traverse this rejection. Solely in an effort to expedite prosecution, and without acquiescing with the propriety of the rejection, however, Applicants have canceled claim 9, thus rendering its rejection moot.

As noted above, the present specification describes a number of representative examples of the claimed genus of muteins and fragments, and provides a detailed description of the functional characteristics of the peptides that would fall within the scope of the claims (see, *e.g.*, Example 2, Table 2; Example 6, Table 3; Example 7, Table 4; and Figures 1-7). Thus, Applicants have clearly met the "representative number" standard under *Eli Lilly* ("[a] description of a genus. . . . may be achieved by means of a recitation of a representative number of [species]. . . . falling within the scope of the genus . . . . " *Regents of Univ. of Calif. v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997)).

Applicants also respectfully disagree with the Examiner's statement that no common structural attributes identify the members of the genus: all the claimed peptides have at least nine out of fourteen amino acids in common, *i.e.*, a common primary structure of the molecule. Moreover, the peptides of the genus all have the same functional characteristics, which are amply described in the specification. Hence, Applicants respectfully assert that the present specification provides sufficient written description to convey to one of ordinary skill that Applicants had possession of the full scope of the claimed invention upon filing of the application.

Applicants wish to remind the Examiner that "[a]dequate description under the first paragraph of 35 U.S.C. 112 does not require *literal* support for the claimed invention . . . . the observation of a lack of literal support does not, in and of itself, establish a *prima facie* case for lack of adequate descriptive support under the first paragraph of 35 U.S.C. 112." *Ex parte*

Parks, 30 USPQ2d 1234, 1236 (Bd. Pat. App. Int. 1994). Instead, the written description requirement of 35 U.S.C. § 112, first paragraph, is met "if the originally-filed disclosure would have conveyed to one having ordinary skill in the art that an [applicant] had possession of the concept of what is claimed," *id.*, *i.e.*, "[i]f a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification . . . ." *In re Alton*, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996). An applicant is not required to disclose or provide a working example of every species of a given genus in order to meet the written description requirement of 35 U.S.C. § 112 (*see Parks* and *Alton*), and subject matter that "might fairly be deduced from the original application" is considered to be described in the application as filed. *Acme Highway Products Corp. v. D.S. Brown Co.*, 431 F.2d 1074, 1080 (6th Cir. 1970) (citations omitted), *cert. denied*, 401 U.S. 956 (1971), *followed by Westphal v. Fawzi*, 666 F.2d 575, 577 (C.C.P.A. 1981). Moreover:

> [t]he purpose of the written description requirement is to prevent an applicant from later asserting that he invented that which he did not; the applicant for a patent is therefore required to "recount his invention in such detail that his future claims can be determined to be encompassed within his original creation."

Amgen Inc. v. Hoechst Marion Roussel, 314 F.3d 1313, 1330 (Fed. Cir. 2003) (citation omitted).

Based on all of the above, the rejection has been overcome. Therefore, Applicants respectfully request that the rejection of claims 2, 8 and 10-12 under 35 U.S.C. § 112, first paragraph be withdrawn.

Applicants note with gratitude that the Examiner has found the currently claimed invention to be patentably distinct over the closest prior art.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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Date: September 17, 2003

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